IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Chang-Yi LIN et al.	Confirmation No: 9676
Appl. No.	: 10/800,622	
Filed	: March 16, 2004	
Title	: STABLE AND TASTE MASKED PHARMACEUTICAL DOSAGE FORM USING POROUS APATITE GRAINS	
TC/A.U.	: 1618	
Examiner	: N.G. Ebrahim	
Docket No.:	: LINC3186CIP/REF	
Customer No:	: 23364	

37 CFR §41.41 REPLY BRIEF

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

This Reply brief is submitted in response to the Examiner's Answer of June 8, 2010 and is therefore timely filed within the two month period for reply. This is responsive to the points raised in the Examiner's Answer.

In the first instance, Appellants note that the claims associated with the rejections have been modified from those from which this appeal has been taken. The rejection of claim 13 as set forth in the first obviousness rejection previously issued has been withdrawn and claim 13 has been added to the second obviousness rejection of claim 12. Claim 13 is dependent on claim 12 and thus the new rejection of claim 13 is not considered a new grounds of rejection.

In addition, Appellants asked for clarification with respect to the rejection of claim 16 in Appellants' Brief and have been advised in the Examiner's Answer with respect to the status of the claims that, claim 16 is rejected, although no grounds of rejection identified.

Claim 1 on Appeal relates to a stable and taste masked pharmaceutical dosage form comprising porous apatite grains and a drug entrapped in pores of said grains,

wherein said grains have a size of 0.1-1000 μm and said pores of said grains have an opening of 0.5-300 nm, (page 3, lines 8-12) and the dosage form further comprising a biocompatible polymer, wherein said porous apatite grains are bound by said biocompatible polymer to form a microspherical composite having a size of 0.5-1000 μm. (Page 4, lines 14-16.)

In order to more clearly illustrate the difference in the claims on Appeal and the revised rejections, Appellants would like to provide a more expansive view on Tsuru's teaching as would be understood by one of ordinary skill in the art with a reasonably broad interpretation of the claimed subject matter. Tsuru's disclosure and claims is to a slow, release drug delivery granules (hereinafter the product) comprising:
porous granules of 1 μm to 10 mm with a drug component impregnated in pores of the granules (claims 1 and 2),
optionally

a) the granules have a hollow structure and an inner space thereof contains the drug component (claim 3);

b) the granules have a coating consisting of a soluble organic polymeric compound applied on a surface thereof (claim 4).

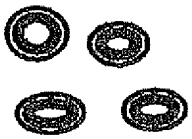
Example 5 of Tsuru is a typical example shows how the porous granules are prepared (TCP fired at 1000°C) and how the drug is impregnated, freeze-dried and disintegrated, and then coated. Example 5 illustrates the above product and the features b).

The above features a) is the technique closest to the subject invention recited in claim 1 of the Appellant's claims on Appeal. Example 6 illustrates this features, wherein spherical acryl beads serving as cores of hydroxyapatite powder were fired at 900°C to form hollow granules of hydroxyapatite, followed by impregnating, freeze-drying and disintegrating, and then coating to obtain the product. Claim 10 of Tsuru recites "burn the combustible substance off, thereby producing the granules having a hollow structure". That is a combustible substance (the spherical acryl beads in Example 6) are burned off to produce a hollow structure of the product.

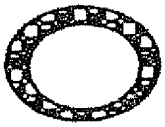
(Note that even at a lower temperature 200 degrees C, the acryl would be removed in accordance with the Tsuru's disclosure despite the Physics law referred to on page 11 of the Examiner's Answer that materials do not evanesce (which means to dissipate like vapor)).

In any case, Tsuru teaches the impregnation is applied to porous granules (with or without the hollow structure), and Tsuru teaches that the coating is applied to the impregnated granules (actually to the dried impregnated granules). The polymer in Tsuru's claim 4, gelatine and chitin in Tsuru's claim 15 and binder in Tsuru's claim 14 are all for forming the coating on the dried impregnated granules. The following drawings show the differences between the product of Tsuru and the microspherical composite recited in the Appellant's claim 1.

Tsuru:



(b) the granules have a coating consisting of a soluble organic polymeric compound applied on a surface thereof (claim 4), wherein the thick lines represent the impregnated granules and the thin lines represent the coating.



a) the granules have a hollow structure and an inner space thereof contains the drug component (claim 3), wherein the central blank represents the hollow structure, the outside circle represents the coating, and the portion between the central blank the outside circle is the impregnated granules.

The Appellant's microspherical composite:

wherein the black dots represent the biocompatible polymer and the blank circles represent the porous apatite grains. As to the drug entrapped in pores of said grains, the Appellants' invention includes an unique process using specific biocompatible polymers (claim 19) to carry it out , i.e. not the impregnation method disclosed by Tsuru. Another unique process (claim 40 not on appeal) is also invented by the Appellants to achieve the goal of "said porous apatite grains are bound by said biocompatible polymer to form a microspherical composite" which is distinctly different from that disclosed in the references applied in the appealed rejection.

Tsuru does not suggest the impregnation is applied to porous granules bounded by a polymer (the microspherical composite of the Appellant's invention). Tsuru does not have a suggestion as to how the microspherical composite of the Appellant's invention is prepared.

The other two references Lee et al (WO 0015194) and Isobe (US 5603945) also do not provide the necessary suggestion as to how the microspherical composite of the Appellant's invention is prepared or even suggested to one of ordinary skill in the art.

Lee cannot remedy the deficiencies of Tsuru which did not disclose binding the granules into composite using a biocompatible polymer," because Lee simply suggests "to use poly-L-lactic acid and/or polyglycolide (PGA) to the granules disclosed by Tsuru to add adjuvancity and/or resorbability to an oral tablet made from the granules disclosed by Tsuru" as indicated by the Examiner, page 5, lines 11-14, of the Examiner's Answer. There is no teaching in Lee as to forming a microspherical composite by using a biocompatible polymer to bind the apatite grains. Instead, Lee teaches "polymer will encapsulate the calcium phosphate adjuvant" in page 20, line 30,

or "biodegradable polymeric microspheres," page 19, line 29, or adjuvant paste injected subcutaneously by adding a supplemental material such as PLA to the hydrated calcium phosphate and mere mixing (Example 35, page 47).

Isobe teaches that "in order to mask the taste and improve the palatability, the edible organic acid or a salt thereof, especially the powdery or granular edible organic acid or a salt thereof, may be coated" as pointed out by the Examiner. The Examiner uses Isobe to assert, "It would have been obvious to a person having ordinary skill in the art at the time the invention was made to use the polymers disclosed by Isobe for taste masking such as cellulose polymers, polyethylene glycol and polyvinyl alcohol to mask the taste and/or improve palatability of drugs such as ascorbic acid." However, this reference does not overcome the deficiencies of the primary reference as discussed above and in the Appeal Brief and the rejection should be reversed or withdrawn.

The second obvious rejection to be reviewed now includes claim 13 in this rejection which previously was of claim 12 under 35 U.S.C. 103 (a) as being unpatentable over Tsuru et al in view of Lee et al and further in view of Makoto et al.

Claim 12 provides that the apatite grains contain carbonate in the amount of 0.1 - 40% based on the weight of the grains. As admitted on page 7 of the final rejection, neither of the references teaches the amount of carbonate in the apatite. The Makoto reference is relied upon for this teaching in this regard, the Examiner's attention is directed to page 10 of Applicant's specification, lines 17-20 wherein it is indicated that seed carbonate bands suggest that the apatite obtained in this composition is AB-type carbonated apatite. Increasing carbonate concentrations suggest sufficient amounts of carbonated ions being incorporated into the apatite lattice.

On the contrary, Otsuka which is the author's last name and Makoto, his first, on page 444 under Materials and Method teaches that tetracalcium phosphate (TTCP) and dicalcium phosphate dihydrate (DCPD) and 0 - 40% (HAP) which is hydroxyapatite seed crystals with various amounts of sodium bicarbonate as summarized in table 1. The cement powder was mixed to form this cement. In the

results and discussion portion on page 446, it is stated that the X-ray diffraction profiles suggest that IMC and sodium bicarbonate did not interfere with the cement setting but apatite formation was deleted by the presence of sodium bicarbonate. Note also the presence of tetracalcium phosphate. It is most respectfully submitted that one of ordinary skill in the art would not find this teaching to a multi-component cement to suggest, as urged in the Examiner's Answer final rejection, that Otsuka et al teaches the inclusion within the apatite grains of carbonate as required by claim 12 on appeal. Especially when combining the teachings of this reference with the teachings of the Tsuru reference for the reasons discussed above. Accordingly, it is most respectfully requested that this rejection be withdrawn or reversed on Appeal.

In view of the above further arguments in response to the Examiner's Answer, the arguments to the appeal rejection, all of the rejections of the claims on appeal should be reversed. The application should be passed to issue.

Respectfully submitted,

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